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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JAGOE, DONNA A	
ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/942,959	OSBAKKEN ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *67-69,73-85,87,90-110,112 and 113* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67-69,73-85,87,90-110,112 and 113* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments filed December 15 2006 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 67-69, 73-85, 87, 90-110, 112 and 113 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 96 and 97 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Regarding the hydrophile-lipophile balance (HLB) of between about 1.8 to about 8.6 in claim **96** and the HLB of between about 9.6 to about 16.7 in claim **97**, when referring to the instant specification, page 24 recites a tutorial of surfactants that act as a solubilizing agent by forming micelles. An HLB value of 10 or higher means that the agent is primarily hydrophilic, while an HLB value of less

than 10 means it would be lipophilic. For example, spans have HLB values ranging from 1.8 to 8.6, which is indicative of oil soluble for oil dispersible molecules. Tweens have HLB values that range from 9.6 to 16.7. This appears to be a tutorial on the actions of Tweens and Spans, rather than specifically envisioned amounts of specific surfactants. The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same. Considering the teachings provided in the specification as originally filed, the Examiner finds that Applicants have failed to provide the necessary teachings, by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formula that fully set for the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that Applicants had possession of the concept of a method of treating chronic sinusitis wherein the surfactant has a hydrophile-lipophile balance (HLB) of between 1.8 to about 8.6 and a method of treating chronic sinusitis wherein surfactant has a HLB of between about 9.6 to about 16.7.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 67-69, 73-85, 90-110, 112 and 113 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rubin et al. U.S. Patent No. 5,925,334 (AE) in view

of Schmitt et al. U.S. Patent No. 4,950,477 (AA) and Saunders Manual of Medical Practice (U)

The claims are drawn to a method of treating sinusitis comprising nasally administering a pharmaceutical composition comprising betamethasone and a surfactant and optionally a second agent selected from the group consisting of an antihistamine, mast cell stabilizer, non-antibiotic anti-microbial agent, an anti-leukotriene, an anti-viral, antiseptic, a non-steroidal anti-inflammatory agent (NSAID), a combination of at least 2 antibiotics, an agent for treating nasal polyps, an anticholinergic agents and combinations thereof.

Rubin et al. teach surfactant such as DPPC and Exosurf ® mixed with an aerosolizing agent to promote mucus clearance (see abstract, see column 4, lines 5-15, see claim 1). The use of the surfactant lowers the surface tension to enhance distribution and spreading of other medications to the lower respiratory tract such as surfactant and an antibiotic and a surfactant and an inhaled anti-inflammatory agent for conditions such as sinusitis (column 10, lines 10-34). Methods of administration of the surfactant composition include a metered dose inhaler, dry powder inhalation, jet nebulization and ultrasonic nebulization (column 9, lines 28-39).

Rubin does not teach particle size, the osmolality, pH or the NaCl equivalency of the composition.

Schmitt et al. teach administration of non-antimicrobial antibiotic such as amphotericin B by aerosol spray to prevent pulmonary infection (column 1, line 60 to column 2, line 4). The particle size of the polyene (amphotericin b) is from 0.5 μm to 8.0

μm. Schmitt et al. teach that the particle size is important because particles smaller than 0.5 μm are exhaled and thus not retained in the lungs while particles greater than 8.0 μm such as those produced in an atomizer do not reach the periphery of the lungs and therefore are not effective in preventing or treating the infection (column 2, lines 48-65).

Schmitt et al. is cited to teach a non-antimicrobial antibiotic and to provide motivation for the instantly claimed particle size. It does not teach treatment of sinusitis and it does not teach osmolality and NaCl equivalency.

Saunders Manual of Medical Practice teach that sinusitis is an inflammation of one or more paranasal sinuses but usually refers to infection of the sinuses (column 1, page 90, 1st paragraph). Further, there may be an overlap between symptoms of acute or chronic sinusitis and other causes of nasal congestion such as allergic or viral rhinitis (column 1, page 90, 4th paragraph). Treatment includes antibiotics such as amoxicillin/clavulanate along with decongestants, mucolytics and other ciliator activators, nasal corticosteroids, antihistamines and saline (pages 91-92).

Saunders Manual is cited to teach the state of the art regarding treatment of sinusitis. It does not teach intra-nasal administration of the agents except the corticosteroids and it does not teach particle size, osmolality and NaCl equivalency of the composition.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made, given the state of the art of the above references to combine the surfactants/antibiotics/anti-inflammatory agents of Rubin et al. with the non-antibiotic

antimicrobial agent and particle size of Schmitt et al. and the other agents disclosed in Saunders Manual of Medical practice such as antibiotics, decongestants, mucolytics, nasal corticosteroids and antihistamines to treat sinusitis with the reasonable expectation of preparing formulations with multiple active agents which make the treatment more effective and potent. Furthermore, one of ordinary skill in the art would be motivated to optimize the osmotic pressure, pH and NaCl equivalency of the composition, by routine experimentation to include a wider range for different drugs.

Applicant asserts that the Examiner relies on Rubin et al. solely for the proposition that surfactants can lower the surface tension to enhance distribution and spreading of other medications to the lower respiratory tract. In response, Rubin et al. teach surfactant such as DPPC and Exosurf ® mixed with an aerosolizing agent to promote mucus clearance (see abstract, see column 4, lines 5-15, see claim 1). The use of the surfactant lowers the surface tension to enhance distribution and spreading of other medications such as surfactant and an antibiotic and a surfactant and an inhaled anti-inflammatory agent for conditions *inter alia* such as **sinusitis** (column 10, lines 10-34). Methods of administration of the surfactant composition include a metered dose inhaler, dry powder inhalation, jet nebulization and ultrasonic nebulization (column 9, lines 28-39).

Regarding the amendment to specify the surface tension of the composition as about 10 to about 70 dynes/cm, as noted in *In re Best* (195 USPQ 430 (CCPA 1977)), and *In re Fitzgerald* (205 USPQ 594 (CCPA 1980)), the mere recitation of newly-discovered function or property, inherently possessed by things in prior art, does not

cause claims drawn to those things to distinguish over prior art. In such a situation, the burden is shifted to the applicant to prove that subject matter shown to be in prior art does not possess characteristic relied on where it has reason to believe that functional limitation asserted to be critical for establishing novelty in claimed subject matter may be inherent characteristic of prior art; whether rejection is based on "inherency" under 35 U.S.C. 102, on "prima facie obviousness" under 35 U.S.C. 103, jointly or alternatively, burden of proof is same.

In holding an invention obvious in view of a combination of references, there must be some suggestion, motivation or teaching in the prior art that would have led a person of ordinary skill in the art to select the references and combine them in the way that would produce the claimed invention. This motivation may flow from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. Here, filtered through prior art, Rubin et al. disclosed that clearance of mucus in the respiratory tract (**including sinusitis** (col. 10, lines 10-34)) can be achieved through inhalation of a surfactant combined with an aerosolizing agent and use of the surfactant lowers the surface tension to enhance distribution and spreading of other medications to the lower respiratory tract such as surfactant and an antibiotic and a surfactant and an inhaled anti-inflammatory agent for conditions such as sinusitis (column 10, lines 10-34). Schmitt et al. teach that the particle size is important because particles smaller than 0.5 μm are exhaled and thus not retained in the lungs while particles greater than 8.0 μm such as those produced in an atomizer do not reach the periphery of the lungs and

therefore are not effective in preventing or treating the infection (column 2, lines 48-65). Saunders Manual is cited to teach the state of the art regarding treatment of sinusitis.

While applicant is correct regarding Schmitt being directed to treatment of lung conditions, the reference is cited to teach the particle size. If inhaled particles smaller than 0.5 μm are not retained in the lungs, it is reasonable to conclude that they would not remain in the sinuses since both the lung lining and the sinus lining would be termed "mucous membranes". Similarly, particles that are greater than 8.0 μm would be expected to not reach the periphery of the sinuses since Schmitt et al teach that such large particle sizes do not reach the periphery of the lungs.

Saunders Manual is cited to teach the state of the art regarding treatment of sinusitis. The agents cited in the instant claims are agents that are all well known in the art, in the treatment of sinusitis. Although the instant claims appear to be first to measure the surface tension in dynes, the HLB value, the NaCl equivalency, and the osmolality, that that discovery does not entitle him to remove the method of treating sinusitis from the public domain. It is noted that the surface tension of about 10 to about 70 dynes/cm includes the surface tension of ordinary **water** (72.8 dynes/cm).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe
Patent Examiner
Art Unit 1614

July 5, 2007

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER